Introductory Comments

I. Summary of the Office Action.

In the Office action, mailed 27 August 2007, the Examiner asserted the following objection and rejections:

The Examiner objected to the disclosure asserting that "[T]he amendments to the description of Figure 2 appear to be new matter. Appropriate correction is required."

The Examiner rejected claims 86-108 under 35 U.S.C. §103(a) asserting that the claims are unpatentable over Parker, et al., WO 00/40273, in view of Goeddel, et al., US 5,120,832, and further in view of Theeuwes, et al., US 4,976,966.

The Examiner rejected claims 86, 97, 103 and 109-113 under 35 U.S.C. §103(a) asserting that the claims are unpatentable over Parker, et al., WO 00/40273, in view of Goeddel, et al., US 5,120,832, and further in view of Theeuwes, et al., US 4,976,966, and Guillen, et al., US 6,074,673.

The Examiner provisionally rejected claims 86-108 on the grounds of non-statutory obviousness-type double patenting as being unpatentable over claims 65 and 86-104 of co-pending Application No.10/982,532.

The objection and rejections are believed to be overcome in part by the amendments and are otherwise traversed for reasons discussed below.

II. Overview of the Amendments.

1. To the Specification.

The amendments to the specification are presented herein below (after the signature page) in the section titled "Amendments to the Specification."

On page 17, ¶0059 is amended. Basis for the amendment can be found throughout the specification, for example, at the following locations: ¶0033; ¶0059 (originally presented); and Figure 2.

Accordingly, no new matter has been added by way of this amendment and the entry thereof is respectfully requested.

2. To the Claims.

Claims 86-113 are pending in the application.

Claims 86, 89, and 97 are canceled by this amendment. Claims 90, 91, 93, 95, 98, and 103-107 are amended without prejudice or disclaimer. Cancellation or amendment of these claims is not intended to be an acquiescence in the Office's assessment of those claims in the Office action, mailed 27 August 2007. Applicant expressly reserves the right to bring the subject matter of the original claims again in a subsequent, related application. New claim 114 is added by this amendment. After entry of this amendment claims 87-88, 90-96, and 98-114 are pending.

No fees for the newly added claim are due as applicant has previously paid fees for a greater number of independent claims and dependent claims than are present in the current claim set.

The amendments to the claims are presented herein below (after the signature page) in the section titled "Amendments to the Claims."

Support for newly presented claim 114 can be found throughout the specification, for example, at the following locations: ¶0002; ¶0030 (second paragraph); ¶0048, page 14, lines 7-9; ¶0053; ¶0055; ; ¶0062; ¶0070 (paragraphs 1-4); ¶0078; ¶0079; ¶0082; ¶0012; and ¶00116.

The amendments to claims 90, 91, 93, 95, 98, and 103-107 are to provide proper antecedent basis for the claims in view of the cancellation of claims 86, 89, and 97.

Accordingly, no new matter has been added by way of this amendment and the entry thereof is respectfully requested.

Remarks

I. Objection to the Specification.

The Examiner objected to the disclosure asserting that "[T]he amendments to the description of Figure 2 appear to be new matter. Appropriate correction is required."

Applicant submits that the previously presented amended language only served to clarify the data presented in Figure 2; however, in view of the Examiner's objection, applicant has restored the specification to the original language presented in ¶0059, with the addition of the phrase "as shown in Figure 2."

Applicant submits that the amendment to the specification does not constitute new matter as ¶0059 describes the data presented in Figure 2 and Figure 2 itself states on the horizontal axis that the dosages are given in micrograms per week (see, Figure 2, "Dose (mcg per week)").

Applicant submits that the current amendment to the specification does not introduce new matter. Withdrawal of the objection to the specification is respectfully requested.

II. Addressing The Examiner's Rejections.

1. Rejection of Claims 86-108 Under 35 U.S.C. §103(a).

The Examiner rejected claims 86-108 under 35 U.S.C. §103(a) asserting that the claims are unpatentable over Parker, et al., WO 00/40273, in view of Goeddel, et al., US 5,120,832, and further in view of Theeuwes, et al., US 4,976,966.

(A) The Combination of References Does Not Teach All of the Elements of the Claimed Invention.

To reject a claim based on combining prior art elements according to known methods to yield predictable results, the Examiner must resolve the Graham factual inquiries. *See Graham v. John Deere Co.*, 383 USC 1, 86 S. Ct. 684, 15 L Ed2d 545, 148 USPQ 459, S. C. 1966. The Examiner must then articulate the following: (1) a finding that the prior art includes each element claimed with the only difference between the claimed invention and the prior art being the lack of actual combination of the elements in a single prior art reference; (2) a finding that one of ordinary skill in the art could have combined the elements as claimed by known methods and that in combination each element merely would

have performed the same function as it did separately; (3) a finding that one of ordinary skill in the art would have recognized that the results of the combination were predictable; and (4) whatever additional findings based on the Graham factual inquiries may be necessary, in view of the facts of the case under consideration, to explain a conclusion of obviousness. (See, Examination Guidelines for Determining Obviousness Under 35 U.S.C. 103 in View of the Supreme Court Decision in *KSR International Co. v. Teleflex Inc.* 57526, 57529 Federal Register / Vol. 72, No. 195.)

The cited references do not teach all of the elements of the independent claims as presented in the accompanying amended claim set. Accordingly, a case of *prima facie* obviousness cannot be established.

First, none of the cited references teaches a method of treating hepatitis C (HCV) in a subject comprising administering a therapeutically effective amount of omega interferon protein to the subject (see, independent claims 87, 88, and 114). The reference of Parker, et al., teaches only the administration of a polynucleotide encoding an omega interferon (see, e.g., Parker, et al., page 3, lines 2-4, lines 26-27, and page 5, lines 11-13). Further, the reference of Parker, et al., presents no data that demonstrate the efficacy of the administration of a polynucleotide encoding omega interferon for the treatment of HCV. Example 6 is a prophetic example written in the present tense. The only virus shown by the reference to be affected by omega interferon is murine encephalomyocarditis virus and only *in vitro* experimental data are given. No anti-viral efficacy of a treatment method using administration of a polynucleotide encoding omega interferon to any animal is taught by the reference. The Examiner notes that the reference of Parker, et al., is "silent regarding administration of omega IFN protein or use of any device for administration" (Office action, mailed 27 August 2007, page 4). The reference of Goeddel, et al., does not teach a method of treating HCV in a subject comprising administering a therapeutically effective amount of omega interferon protein to the subject. As noted by the Examiner, "Goeddel *et al* does not specifically teach administration of omega IFN for treatment of HCV infection" (Office action, mailed 27 August 2007, page 4). Finally, the reference of Theeuwes, et al., does not teach a method of treating HCV in a subject comprising administering a therapeutically effective amount of omega interferon protein to the subject.

Second, none of the cited references teaches or suggests the administration of omega interferon protein at the claimed microgram per week dosage ranges. The reference of Parker, et al., teaches only the administration of constructs comprising polynucleotides encoding omega interferon. It is notoriously difficult in the field of gene therapy in animals to control and maintain a predetermined range of expressed polypeptide over time from constructs comprising polynucleotides encoding polypeptides. Low levels of gene expression and lack of control of gene expression are generally recognized as limiting the clinical success of gene therapy methods such as those disclosed by the reference of Parker, et al. The Examiner suggests that regarding "the claimed dosages, timing of administration, or routes of administration, a person of ordinary skill in the art would have both the motivation and the ability to optimize these variables to practice the most effective method of treatment" (see, Office action, mailed 27 August 2007, page 5). However, the Examiner presents no evidence to support this assertion. Further, the treatment of HCV has been recalcitrant to treatment and even the most successful prior art treatment method using alpha interferon (with or without Ribavirin) produced subjects having chronic HCV infection resistant to the treatment method (see, e.g., the present specification, ¶0007; see also, Buckwold, et al., page 118, cols. 1-2, a copy of which accompanies this response). As demonstrated in the present application, even such subjects having chronic HCV infection resistant to treatment with alpha interferon (with or without Ribavirin) show clearance of HCV in response to the treatment methods of the present invention (see, e.g., the present specification, ¶0058-¶0059). Further, neither of the secondary references teaches or suggests the administration of omega interferon protein at the claimed microgram per week dosage ranges. As noted by the Examiner, "the combination of Parker *et al*, Goeddel *et al*, and Theeuwes *et al* does not specifically recite the claimed dosages, timing of administration, or routes of administration" (see, Office action, mailed 27 August 2007, page 5).

The dependent claims distinguish over the combination of references by virtue of their incorporation of the limitations of the independent claim from which they depend.

Accordingly, applicant submits that the Examiner has failed to establish a case of *prima facie* obviousness for the presently claimed invention as none of the cited references teaches the elements of the claimed invention. In view of the above-presented arguments,

applicant respectfully requests that the rejection under 35 U.S.C. §103 be withdrawn.

(B) The Primary Reference Teaches Away From the Claimed Invention.

Even if, *in arguendo*, the elements of the invention are taught by the prior art obviousness cannot be established if the prior art teaches away from the claimed invention. The Examination Guidelines for Determining Obviousness Under 35 U.S.C. 103 in View of the Supreme Court Decision in *KSR International Co. v. Teleflex Inc.* (57526, at 57529 Federal Register / Vol. 72, No. 195) state the following:

> "Note that combining known prior art elements is not sufficient to render the claimed invention obvious if the results would not have been predictable to one of ordinary skill in the art." (Regarding "teaching away" the guidelines cite, *United States v. Adams*, 383 U.S. 39, 51–52, 148 USPQ 479, 483 (1966), wherein the Supreme Court would not require that one of ordinary skill in the art ignore the teaching away of the prior art.).

As discussed herein above, the primary reference of Parker, et al., teaches only the administration of a polynucleotide encoding an omega interferon (see, e.g., Parker, et al., page 3, lines 2-4, lines 26-27, and page 5, lines 11-13). In fact, the reference of Parker, et al., notes that "IFN-omega has never been used for the treatment of infectious diseases, even in the form of a recombinant protein" (Parker, et al., page 2, lines 11-12). Further, the reference of Parker, et al., states "[T]reatment of infectious diseases with an interferon (IFN) has traditionally involved repeat injections of large doses of recombinant protein" (Parker, et al., page 1, lines 10-11). The reference goes on to state "[C]learly, there is a need for an improved delivery system for treating infectious diseases with IFNs." Following this introduction, all of the teachings of the reference of Parker, et al., are directed to the treatment of infectious disease by administering a polynucleotide construct into a tissue of a mammal and the advantages thereof. The reference does not teach a method involving direct administration of omega interferon protein nor any advantage to such a method.

A reference should be considered as a whole, and portions arguing against or teaching away from the claimed invention must be considered. *See, e.g., Bausch & Lomb v. Barnes-Hind/Hydrocurve*, 796 F.2d 443, 230 USPQ 416 (CAFC 1986). Prior art may be considered not to teach an invention, and thereby fail to support an obviousness rejection, when the stated objectives of the prior art reinforce such an interpretation. *See, e.g., WMS Gaming Inc.*

v. International Game Tech, 184 F.3d 1339, 51 USPQ2d 1385, 1400 (Fed. Cir. 1999). In the present situation, the stated objective of the reference of Parker, et al., is to provide an improved delivery system for treating infectious diseases with interferons wherein the system is the delivery of polynucleotides encoding omega interferon. Accordingly, the reference of Parker, et al., teaches away from the methods of the present invention that use administration of a therapeutically effective amount of omega interferon protein to a subject. Applicant submits that modification of the reference of Parker, et al., to achieve a contrary purpose to the stated objective of the reference is inappropriate and does not support a conclusion of obviousness. None of the cited secondary references makes up for this shortcoming of the reference of Parker, et al.

The dependent claims distinguish over the combination of references by virtue of their incorporation of the limitations of the independent claim from which they depend.

Accordingly, applicant submits that the Examiner has failed to establish a case of *prima facie* obviousness for the presently claimed invention as modification of the reference of Parker, et al., along the lines suggested by the Examiner is counter to the stated intention of the reference. In view of the above-presented arguments, applicant respectfully requests that the rejection under 35 U.S.C. §103 be withdrawn.

(C) Secondary Considerations.

In *KSR Int'l Co. v. Teleflex Inc.*, 127 S. Ct. 1727; 167 L. Ed. 2d 705; 2007 U.S. LEXIS 4745; 75 U.S.L.W. 4289; 82 USPQ.2D 1385 (S.Ct. 2007), the Supreme Court reaffirmed use of the Graham factors in the determination of obviousness under 35 U.S.C. §103(a). The four factual inquiries under Graham are: (a) determining the scope and contents of the prior art; (b) ascertaining the differences between the prior art and the claims in issue; (c) resolving the level of ordinary skill in the pertinent art; and (d) evaluating evidence of secondary consideration. *See Graham v. John Deere Co.*, 383 U.S. 1, 17-18, 86 S. Ct. 684, 15 L. Ed. 2d 545, 148 USPQ 459, 467 (S.Ct. 1966).

The reference of Parker, et al., presents no data that demonstrate the efficacy of the administration of a polynucleotide encoding omega interferon for the treatment of HCV. The single example related to treatment of HCV is a prophetic example. In addition, as noted

above, the reference of Parker, et al., does not teach a method of treating HCV in a subject comprising administering a therapeutically effective amount of omega interferon protein to the subject. On the other hand, applicant's specification teaches not only that administration of omega interferon protein is efficacious for the treatment of HCV (see, e.g., ¶0059 and Figure 2) but also that administration of omega interferon protein is efficacious for the treatment of HCV in individual subjects with chronic HCV resistant to treatment with alpha interferon (with or without Ribavirin). This advantage of present invention was unrecognized in the prior art. Further, as stated by the reference of Buckwold, et al., treatment of subjects with omega interferon protein is well tolerated (see, e.g., Abstract and page 119, col. 1, first full paragraph). This presents another advantage of the treatment method of the present invention.

In addition, as stated in the reference of Buckwold, et al., "[O]ther antiviral therapies to treat HCV-infected patients are desperately needed" (page 118, col. 2). The present invention provides such antiviral therapy and the methods of treatment disclosed in the present specification are consistent with the teachings of the reference of Buckwold, et al., concerning the antiviral activity of omega interferon against HCV.

Accordingly, these unappreciated and unexpected advantages of the present invention should be evaluated in the context of any asserted rejection under 35 U.S.C. §103(a). Applicant submits that the Examiner has not addressed these secondary considerations and respectfully requests their consideration.

2. Rejection of Claims 86, 97, 103 and 109-113 Under 35 U.S.C. §103(a).

The Examiner rejected claims 86, 97, 103 and 109-113 under 35 U.S.C. §103(a) asserting that the claims are unpatentable over Parker, et al., WO 00/40273, in view of Goeddel, et al., US 5,120,832, and further in view of Theeuwes, et al., US 4,976,966, and Guillen, et al., US 6,074,673.

Claims 86, 89, and 97 are canceled by this amendment. Claims 103 and 109-113 all ultimately depended from claim 86. Cancellation of claim 86 obviates this rejection.

The combination of references, as discussed herein above, does not teach all of the elements of the claimed invention. In order for a combination of references to render

obvious a claimed invention, all of the recited elements of claimed invention must be taught by the combination of references. Further, the combination of references does not render the presently claimed invention obvious because the primary reference teaches away from the present invention as discussed herein above. Accordingly, the Examiner has failed to establish a case of *prima facie* obviousness for independent claims 87, 88 and 114. Claim 97 is canceled. Claims 103 and 109-113 all now depend from claim 87. The dependent claims distinguish over the combination of references by virtue of their incorporation of the limitations of the independent claim from which they depend.

Accordingly, applicant submits that the Examiner has failed to establish a case of *prima facie* obviousness. In view of the above-presented arguments, applicant respectfully requests that the rejections under 35 U.S.C. §103 be withdrawn.

3. Provisional Rejection Of Claims 86-108 On The Grounds Of Non-statutory Obviousness-Type Double Patenting.

The Examiner provisionally rejected claims 86-108 on the grounds of non-statutory obviousness-type double patenting as being unpatentable over claims 65 and 86-104 of co-pending Application No.10/982,532.

As this is a provisional obviousness-type double patenting rejection, applicant respectfully requests that this rejection be held in abeyance until agreement on allowable subject matter is established in the present application or in co-pending Application No. 10/982,532. Applicant notes that co-pending Application No. 10/982,532 is commonly owned with the present application by Intarcia Therapeutics, Inc.

III. Supplemental Information Disclosure Statement.

Accompanying this paper is a Supplemental Information Disclosure Statement. Applicant requests that the Examiner indicate that the references have been considered and are of record by initialing each cited reference on the accompanying modified form 1449 and returning a copy of the initialed form to the applicant.

IV. Conclusion.

Applicant respectfully submits that the claims comply with the requirements of 35 U.S.C. §112 and define an invention that is patentable over the art.

Please direct all further communications in this application to:

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If the Examiner notes any further matters which the Examiner believes may be expedited by a telephone interview, the Examiner is requested to contact the undersigned at (650) 780-9030.

Respectfully submitted,

Dated: 28 January 2008 By : Gary R Fabian

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